PCT/EP 00 / 08143 #2

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Dated 21 August 2000

GB9919499.5

By virtue of a direction given under Section 30 of the Patents Act 1977, the application is proceeding in the name of

AVENTIS CROPSCIENCE GMBH,
Brüningstrasse 50,
65929 Frankfurt am Main,
Federal Republic of Germany

[ADP No. 07950702001]

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1. Your reference 99c111

2. Patent application number *(The Patent Office will fill in this part)* 18 AUG 1999 **9919499.5**

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

Hoechst Schering AgrEvo GmbH
Miraustr. 54
D-13509 Berlin
Germany

SECTION 30(1)(97 ACT) APPLICATION FILED 17/7/00.

Patents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of its incorporation Germany 6696462001

4. Title of the invention

FUNGICIDAL COMPOUNDS.

5. Name of your agent *(if you have one)*

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

Aventis CropScience
~~AgrEvo~~ UK Limited
Patent Department
~~Chesterford Park~~ Fyfield Road
~~Saffron Walden~~ Ongar
~~Essex CB10 1XL~~ Essex CM5 0HW

51/1n 16.8.00 dl

Patents ADP number *(if you know it)* 6512040003

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Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

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a) any applicant named in part 3 is not an inventor, or
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11. I/We request the grant of ~~a patent~~ on the basis of this application.

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P.C. SEWELL

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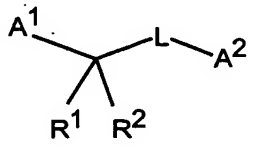
Fungicid s

This invention relates to compounds having fungicidal activity.

In a first aspect the invention provides the use of a compound of general formula I and salts thereof as phytopathogenic fungicides



(I)

where

A^1 is 2-pyridyl or its *N*-oxide, each of which may be substituted by up to four groups at least one of which is haloalkyl;

A^2 is heterocyclyl or carbocyclyl, each of which may be substituted (A^2 is preferably optionally substituted phenyl, optionally substituted heterocyclyl, optionally substituted cyclohexyl or optionally substituted cyclopropyl);

L is a 3-atom linker, selected from the list: $-N(R^5)C(=X)N(R^6)-$, $-N(R^5)C(=X)CH(R^3)-$, $-CH(R^3)N(R^5)CH(R^4)-$, $-CH(R^3)N(R^5)C(=X)-$, $-N(R^3)CH(R^4)C(=X)-$ or $-O-N(R^5)C(=X)-$; wherein A^1 is attached to the left hand side of linker L;

where R^1, R^2, R^3 and R^4, which may be the same or different, are R^b, cyano, nitro, halogen, $-OR^b$, $-SR^b$ or optionally substituted amino (R^1, R^2, R^3 and R^4 are preferably hydrogen, optionally substituted alkyl, optionally substituted phenyl, cyano, acyl and halogen);

R^5 and R^6 which may be the same or different, are R^b, cyano or nitro; or any R^1, R^3 or R^5 group, together with the interconnecting atoms, can form a 3-, 4- 5- or 6-membered ring with any R^2, R^4 or R^6 or any R^1, R^2, R^3, R^4, R^5 or R^6 group, together with the interconnecting atoms can form a 5- or 6-membered ring with A^2 (R^5 and R^6 are pr ferably hydrogen, optionally substituted alkyl or acyl);

X is oxygen or sulfur;

wherein R^b is alkyl, alkenyl, alkynyl, carbocyclyl or h terocyclyl, each of which may be substituted, or hydrogen or acyl.

Preferred substituents on the 2-pyridyl group (A^1) are halogen, hydroxy, cyano, nitro, SF_5, trialkylsilyl, optionally substituted amino, acyl, or a group $-R^a$, $-OR^a$ or $-SR^a$, or a group $-C(R^a)=N-Q$, where Q is $-R^a$, $-OR^a$, $-SR^a$ or optionally substituted amino, wherein R^a is alkyl, alkenyl, alkynyl, carbocyclyl or heterocyclyl, each of which may be substituted; or two adjacent substituents together with the atoms to which they are attached form an optionally substituted ring which can contain up to 3 hetero atoms. Especially preferred substituents are alkoxy, alkyl, cyano, halogen, nitro, alkoxycarbonyl, alkylsulfinyl, alkylsulfonyl and trifluoromethyl, particularly chlorine and trifluoromethyl.

Preferably, the 2-pyridyl group is substituted at the 3 and/or 5 position.

The invention also includes any of the compounds specifically exemplified hereinafter.

Any alkyl group may be straight or branched and is preferably of 1 to 10 carbon atoms, especially 1 to 7 and particularly 1 to 5 carbon atoms.

Any alkenyl or alkynyl group may be straight or branched and is preferably of 2 to 7 carbon atoms and may contain up to 3 double or triple bonds which may be conjugated, for example vinyl, allyl, butadienyl or propargyl.

Any carbocyclyl group may be saturated, unsaturated or aromatic, and contain 3 to 8 ring-atoms. Preferred saturated carbocyclyl groups are cyclopropyl, cyclopentyl or cyclohexyl. Preferred unsaturated carbocyclyl groups contain up to 3 double bonds. A preferred aromatic carbocyclyl group is phenyl. The term carbocylic should be similarly construed. In addition, the term carbocyclyl includes any fused combination of carbocyclyl groups, for example naphthyl, phenanthryl, indanyl and indenyl.

Any heterocyclyl group may b saturated, unsaturated or aromatic, and contain 5 to 7 ring-atoms up to 4 of which may be hetero-atoms such as nitrogen, oxygen and sulfur. Examples of heterocyclyl groups are furyl, thienyl, pyrrolyl, pyrrolinyl, pyrrolidinyl, imidazolyl, dioxolanyl, oxazolyl, thiazolyl, imidazolyl, imidazolinyl, imidazolidinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyranyl, pyridyl, piperidinyl, dioxanyl, morpholino, dithianyl, thiomorpholino, pyridazinyl, pyrimidinyl, pyrazinyl, piperazinyl, sulfolanyl, tetrazolyl, triazinyl, azepinyl, oxazepinyl, thiazepinyl, diazepinyl and thiazolinyl. In addition, the term heterocyclyl includes fused heterocyclyl groups, for example benzimidazolyl, benzoxazolyl, imidazopyridinyl, benzoxazinyl, benzothiazinyl, oxazolopyridinyl, benzofuranyl, quinolinyl, quinazolinyl, quinoxalinyl, dihydroquinazolinyl, benzothiazolyl, phthalimido, benzofuranyl, benzodiazepinyl, indolyl and isoindolyl. The term heterocyclic should be similarly construed.

Any alkyl, alkenyl, alkynyl, carbocyclyl or heterocyclyl group, when substituted, may be substituted by one or more substituents, which may be the same or different, and may be selected from the list: hydroxy; mercapto; azido; nitro; halogen; cyano; acyl; optionally substituted amino; optionally substituted carbocyclyl; optionally substituted heterocyclyl; cyanato; thiocyanato; $-SF_5$; $-OR^a$; $-SR^a$ and $-Si(R^a)_3$, where R^a is alkyl, alkenyl, alkynyl, carbocyclyl or heterocyclyl, each of which may be substituted. In the case of any carbocyclyl or heterocyclyl group the list includes additionally: alkyl, alkenyl and alkynyl, each of which may be substituted. Preferred substituents on any alkyl, alkenyl or alkynyl group are alkoxy, haloalkoxy or alkylthio, each containing 1 to 5 carbon atoms; halogen; or optionally substituted phenyl. Preferred substituents on any carbocyclyl or heterocyclyl group are alkyl, haloalkyl, alkoxy, haloalkoxy or alkylthio, each containing 1 to 5 carbon atoms; halogen; or optionally substituted phenyl.

In the case of any alkyl group or any unsaturated ring-carbon in any carbocyclyl or heterocyclyl group the list includes a divalent group such as oxo or imino, which may be substituted by optionally substituted amino, R^a or $-OR^a$. Preferred groups are oxo, imino, alkylimino, oximino, alkyloximino or hydrazono.

Any amino group, when substituted and where appropriate, may be substituted by one or two substituents which may be the same or different, selected from the list: optionally substituted alkyl, optionally substituted amino, $-OR^a$ and acyl groups. Alternatively two substituents together with the nitrogen to which they are attached may form a heterocyclyl group, preferably a 5 to 7-membered heterocyclyl group, which may be substituted and may contain other hetero atoms, for example morpholino, thiomorpholino or piperidinyl.

The term acyl includes the residues of sulfur and phosphorus-containing acids as well as carboxylic acids. Typically the residues are covered by the general formulae $-C(=X^a)R^c$, $-S(O)_pR^c$ and $-P(=X^a)(OR^a)(OR^a)$, where appropriate X^a is O or S, R^c is as defined for R^a, $-OR^a$, $-SR^a$, optionally substituted amino or acyl; and p is 1 or 2. Preferred groups are $-C(=O)R^d$, $-C(=S)R^d$, and $-S(O)_pR^d$ where R^d is alkyl, C_1 to C_5 alkoxy, C_1 to C_5 alkylthio, phenyl, heterocyclyl or amino, each of which may be substituted.

Complexes of compounds of the invention are usually formed from a salt of formula MAn_2, in which M is a divalent metal cation, e.g. copper, manganese, cobalt, nickel, iron or zinc and An is an anion, e.g. chloride, nitrate or sulfate.

In cases where the compounds of the invention exist as the E and Z isomers, the invention includes individual isomers as well as mixtures thereof.

In cases where compounds of the invention exist as tautomeric isomers, the invention includes individual tautomers as well as mixtures thereof.

In cases where the compounds of the invention exist as optical isomers, the invention includes individual isomers as well as mixtures thereof.

The compounds of the invention have activity as fungicides, especially against fungal diseases of plants, e.g. mildews and particularly cereal powdery mildew (*Erysiphe graminis*) and vine downy mildew (*Plasmopara viticola*), rice blast (*Pyricularia oryzae*), cereal eyespot (*Pseudocercosporella herpotrichoides*), rice

sheath blight (*Pellicularia sasakii*), grey mould (*Botrytis cinerea*), damping off (*Rhizoctonia solani*), wheat brown rust (*Puccinia recondita*), late tomato or potato blight (*Phytophthora infestans*), apple scab (*Venturia inaequalis*), and glume blotch (*Leptosphaeria nodorum*). Other fungi against which the compounds may be active include other powdery mildews, other rusts, and other general pathogens of Deuteromycete, Ascomycete, Phycomycete and Basidomycete origin.

The invention thus also provides a method of combating fungi at a locus infested or liable to be infested therewith, which comprises applying to the locus a compound of formula I.

The invention also provides an agricultural composition comprising a compound of formula I in admixture with an agriculturally acceptable diluent or carrier.

The composition of the invention may of course include more than one compound of the invention.

In addition, the composition can comprise one or more additional active ingredients, for example compounds known to possess plant-growth regulant, herbicidal, fungicidal, insecticidal, acaricidal, antimicrobial or antibacterial properties. Alternatively the compound of the invention can be used in sequence with the other active ingredient.

The diluent or carrier in the composition of the invention can be a solid or a liquid optionally in association with a surface-active agent, for example a dispersing agent, emulsifying agent or wetting agent. Suitable surface-active agents include anionic compounds such as a carboxylate, for example a metal carboxylate of a long chain fatty acid; an *N*-acylsarcosinate; mono- or di-esters of phosphoric acid with fatty alcohol ethoxylates or alkyl phenol ethoxylates or salts of such esters; fatty alcohol sulfates such as sodium dodecyl sulfate, sodium octadecyl sulfate or sodium cetyl sulfate; ethoxylated fatty alcohol sulfates; ethoxylated alkylphenol sulfates; lignin sulfonates; petroleum sulfonates; alkyl-aryl sulfonates such as alkyl-benzene sulfonates or lower alkylnaphthalene sulfonates, e.g. butyl-naphthalene sulfonate; salts of sulfonated naphthalene-formaldehyde

condensates; salts of sulfonated phenol-formaldehyde condensates; or more complex sulfonates such as the amide sulfonates, e.g. the sulfonated condensation product of oleic acid and *N*-methyl taurine; the dialkyl sulfosuccinates, e.g. the sodium sulfonate of dioctyl succinate; acid derivatives of alkyl glycosides and alkylpolyglycosides materials and their metal salts, e.g. alkyl polyglycoside citrate or tartrate materials; or mono-, di- and tri-alkyl esters of citric acid and their metal salts.

Nonionic agents include condensation products of fatty acid esters, fatty alcohols, fatty acid amides or fatty-alkyl- or alkenyl-substituted phenols with ethylene and/or propylene oxide; fatty esters of polyhydric alcohol ethers, e.g. sorbitan fatty acid esters; condensation products of such esters with ethylene oxide, e.g. polyoxyethylene sorbitan fatty acid esters; alkyl glycosides, alkyl polyglycoside materials; block copolymers of ethylene oxide and propylene oxide; acetylenic glycols such as 2,4,7,9-tetramethyl-5-decyne-4,7-diol, ethoxylated acetylenic glycols; acrylic based graft copolymers; alkoxylated siloxane surfactants; or imidazoline type surfactants, e.g. 1-hydroxyethyl-2-alkylimidazoline.

Examples of a cationic surface-active agent include, for instance, an aliphatic mono-, di-, or polyamine as an acetate, naphthenate or oleate; an oxygen-containing amine such as an amine oxide, polyoxyethylene alkylamine or polyoxypropylene alkylamine; an amide-linked amine prepared by the condensation of a carboxylic acid with a di- or polyamine; or a quaternary ammonium salt.

The compositions of the invention can take any form known in the art for the formulation of agrochemicals, for example, a solution, an aerosol, a dispersion, an aqueous emulsion, a microemulsion, a dispersible concentrate, a dusting powder, a seed dressing, a fumigant, a smoke, a dispersible powder, an emulsifiable concentrate, granul s or an impregnated strip. Moreover it can be in a suitable form for direct application or as a concentrate or primary composition which requires dilution with a suitable quantity of water or other diluent before application.

A dispersible concentrate comprises a compound of the invention dissolved in one or more water miscible or semi-water miscible solvents tog ther with one or more surface activeand/or polymeric material. Addition of the formulation to water results in the crystalisation of the active ingredient, the process being controlled by the surfactants and/or polymers resulting in a fine dispersion.

A dusting powder comprises a compound of the invention intimately mixed and ground with a solid pulverulent diluent, for example, kaolin.

An emulsifiable concentrate comprises a compound of the invention dissolved in a water-immiscible solvent which forms an emulsion or microemulsion on addition to water in the presence of an emulsifying agent.

A granular solid comprises a compound of the invention associated with similar diluents to those that may be employed in dusting powders, but the mixture is granulated by known methods. Alternatively it comprises the active ingredient absorbed or coated on a pre-formed granular carrier, for example, Fuller's earth, attapulgite, silica or limestone grit.

Wettable powders, granules or grains usually comprise the active ingredient in admixture with suitable surfactants and an inert powder diluent such as clay or diatomaceous earth.

Another suitable concentrate is a flowable suspension concentrate which is formed by grinding the compound with water or other liquid, surfactants and a suspending agent.

The concentration of the active ingredient in the composition of the present invention, as applied to plants is preferably within the range of 0.0001 to 1.0 per cent by weight, especially 0.0001 to 0.01 per cent by weight. In a primary composition, the amount of active ingredient can vary widely and can be, for example, from 5 to 95 per cent by weight of the composition.

The invention is generally applied to seeds, plants or their habitat. Thus, the compound can be applied directly to the soil before, at or after drilling so that the

presence of active compound in the soil can control the growth of fungi which may attack seeds. When the soil is treated directly the active compound can be applied in any manner which allows it to be intimately mixed with the soil such as by spraying, by broadcasting a solid form of granules, or by applying the active ingredient at the same time as drilling by inserting it in the same drill as the seeds. A suitable application rate is within the range of from 5 to 1000 g per hectare, more preferably from 10 to 500 g per hectare.

Alternatively the active compound can be applied directly to the plant by, for example, spraying or dusting either at the time when the fungus has begun to appear on the plant or before the appearance of fungus as a protective measure. In both such cases the preferred mode of application is by foliar spraying. It is generally important to obtain good control of fungi in the early stages of plant growth, as this is the time when the plant can be most severely damaged. The spray or dust can conveniently contain a pre- or post-emergence herbicide if this is thought necessary. Sometimes, it is practicable to treat the roots, bulbs, tubers or other vegetative propagule of a plant before or during planting, for example, by dipping the roots in a suitable liquid or solid composition. When the active compound is applied directly to the plant a suitable rate of application is from 0.025 to 5 kg per hectare, preferably from 0.05 to 1 kg per hectare.

In addition, the compounds of the invention can be applied to harvested fruits, vegetables or seeds to prevent infection during storage.

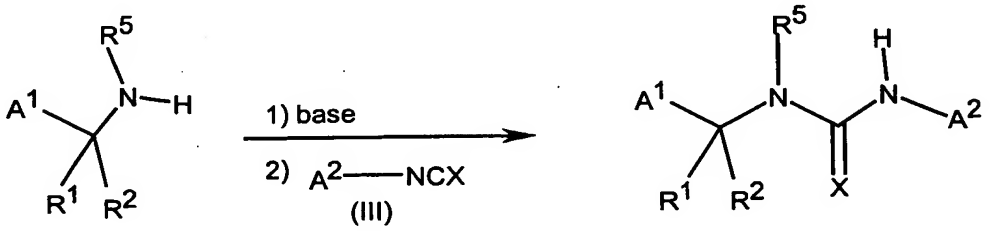
In addition, the compounds of the invention can be applied to plants or parts thereof which have been genetically modified to exhibit a trait such as fungal and/or herbicidal resistance.

In addition the compounds of the invention can be used to treat fungal infestations in timber and in public health applications. Also the compounds of the invention can be used to treat insect and fungus infestations in domestic and farm animals.

Compounds of the invention may be prepared, in known manner, in a variety of ways.

Compounds of formula Ia, i.e. compounds of general formula I where L is $-N(R^5)C(=X)NH-$, can be prepared by reacting compounds of formula II or their hydrochloride salt, with compounds of formula III according to reaction scheme 1. A preferred base is triethylamine.

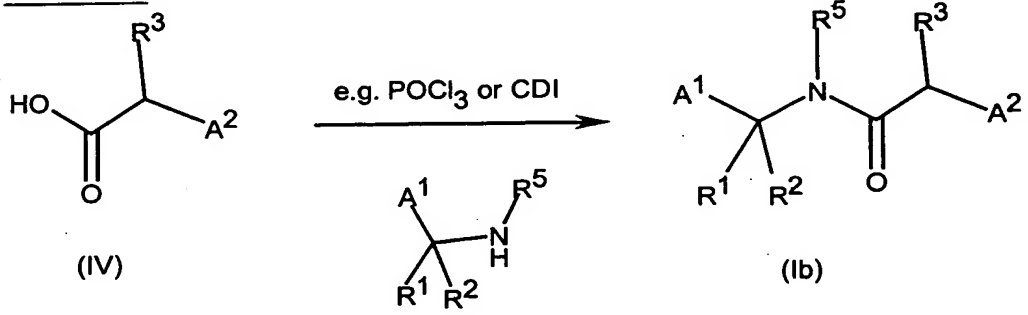
Scheme 1



(II) (Ia)

Compounds of formula Ib, i.e. compounds of general formula I where L is $-N(R^5)C(=O)CH(R^3)-$, may be prepared by reacting compounds of formula IV with compounds of formula II according reaction scheme 2. A variety of methods are available to the chemist, for example, generation of the acid chloride of IV, using reagents such as phosphoryl chloride or oxalyl chloride, followed by addition of II. Alternatively, carbonyl diimidazole (CDI) can be used to activate compounds of formula IV prior to addition of II.

Scheme 2



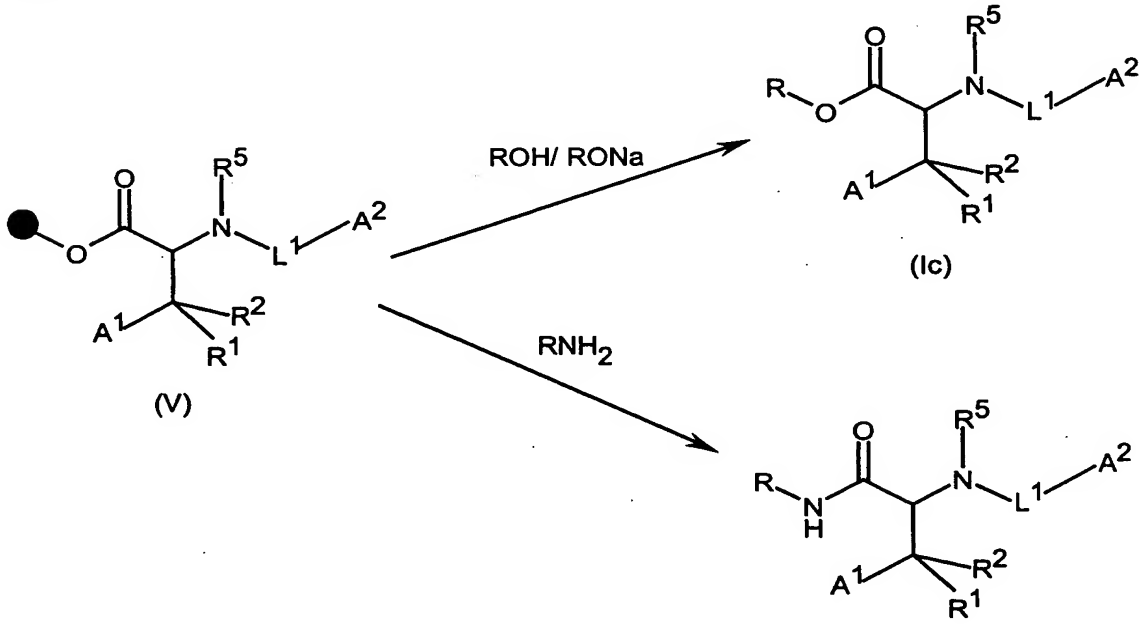
(IV) (II) (Ib)

Collections of compounds of formula (I) may also be prepared in a parallel manner, either manually, automatically or semi-automatically. This parallel preparation may be applied to the reaction procedure, work-up or purification of products or intermediates. For a review of such procedures see by S.H. DeWitt in "Annual Reports in Combinatorial Chemistry and Molecular Diversity: Automated synthesis", Volume 1, Verlag Escom 1997, pages 69 to 77.

Furthermore, compounds of the formula (I) may be prepared using solid-supported methods, where the reactants are bound to a synthetic resin. See for example: Barry A. Bunin in "The Combinatorial Index", Academic Press, 1998 and "The tea-bag method" (Houghten, US 4,631,211; Houghten et al., Proc. Natl. Acad. Sci, 1985, 82, 5131-5135).

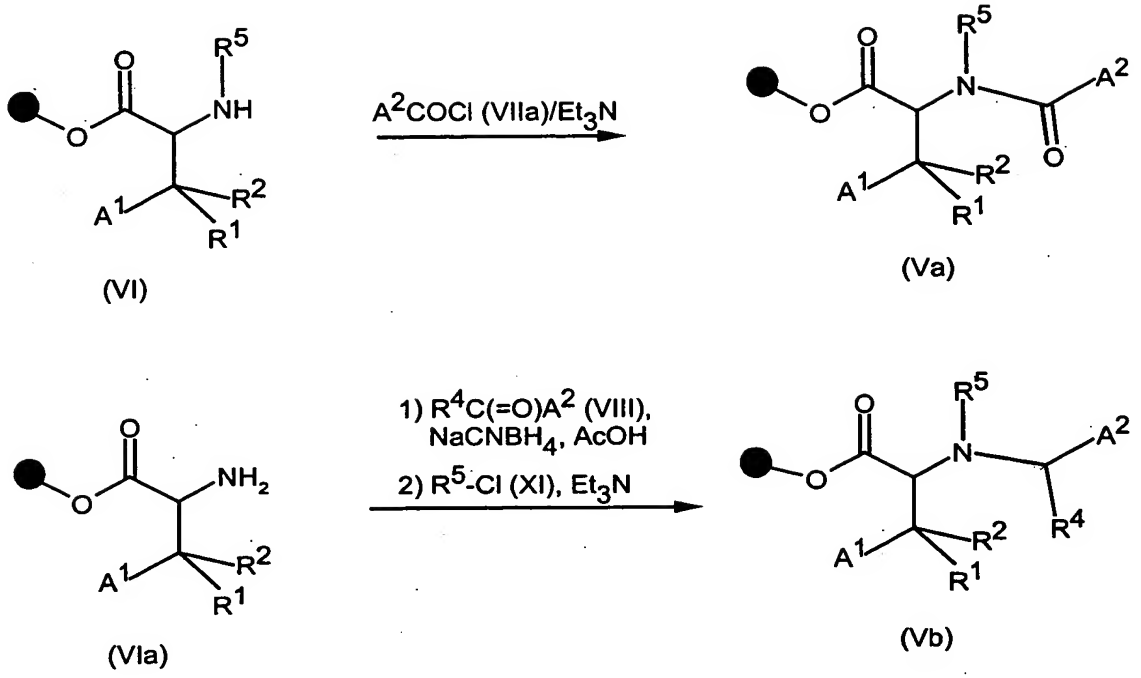
Compounds of formula Ic and Id, i.e. compounds of general formula I where L is $-CH(R^3)-N(R^5)-L^1-$ and L^1 is $-C(=X)-$ or $-CH(R^4)-$, wherein R^3 is alkoxycarbonyl or carbamoyl respectively, can be prepared by various methods known to the skilled chemist. In particular, compounds of formula Ic or Id may be prepared from solid supported reagents of formula V according to reaction scheme 3, wherein the black circle represents Merrifield resin.

Scheme 3



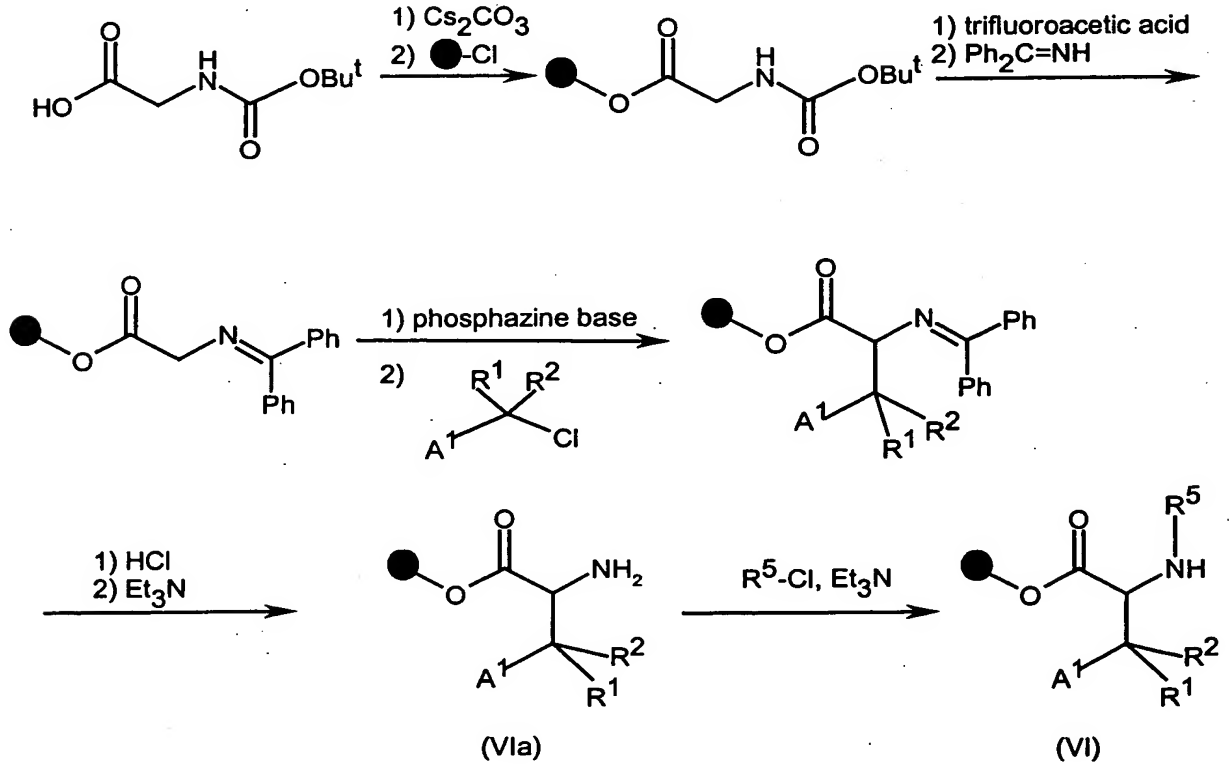
Compounds of formula V may be prepared in turn from compounds of formula VI, by methods analogous to that depicted in reaction scheme 4. Compounds of formula Va may be prepared by treating VI with a compound of formula VIIa in the presence of a suitable base, such as triethylamine. Compounds of formula Vb may be prepared from compounds of formula Via by treatment with compounds of formula VIII, sodium cyanoborohydride and acetic acid followed by reaction with compounds of formula IX and triethylamine

Scheme 4



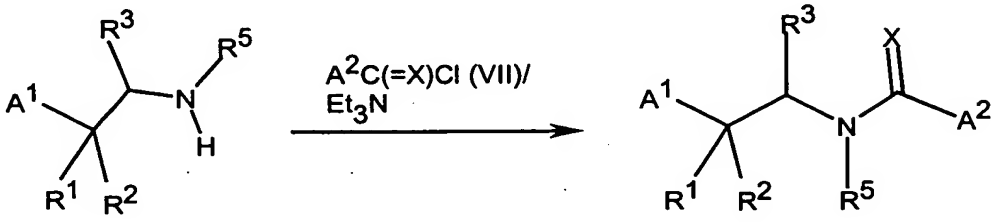
Compounds of formula VI can be prepared using similar methods to reaction scheme 5.

Scheme 5



Compounds of formula Ie, i.e. compounds of general formula I where L is $-CH(R^3)N(R^5)C(=X)-$ may be prepared by reacting compounds of formula X with compounds of formula VII according to reaction scheme 5.

Scheme 5



(X) (Ie)

Other methods will be apparent to the chemist skilled in the art, as will be the methods for preparing starting materials and intermediates.

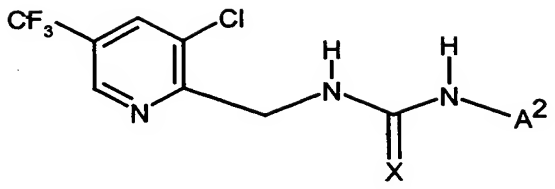
The invention is illustrated in the following Examples. Structures of isolated, novel compounds were confirmed by ^1H NMR (in $CDCl_3$) and/or other appropriate analyses.

Example 1

N-(2-Chlorophenyl)-*N'*-[(3-chloro-5-trifluoromethyl-2-pyridyl)methyl]thiourea (Compound 30)

To a suspension of (3-chloro-5-trifluoromethyl-2-pyridyl)methylamine hydrochloride (0.12 g) and 2-chlorophenylisothiocyanate (0.09 g) in dry tetrahydrofuran (10 ml) was added 10 drops of triethylamine. The mixture was stirred at room temperature overnight. The solvent was removed by evaporation *in vacuo* and the residue extracted with ethyl acetate and washed with 2M hydrochloric acid. The layers were separated and the organic phase was evaporated to dryness to give the title product, m.p. 126 °C.

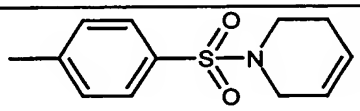
The following compounds of formula If (see Table A), i.e. compounds of general formula I where A^1 is 3-Cl-5-CF_3-2-pyridyl, R^1 and R^2 are hydrogen and L is $-NHC(=X)NH-$, may be prepared by methods analogous to those of Example 1.



(If)

Table A

Cmp	X	A^2	Characterising data
1	O	phenyl	m.p. 143-6 °C
2	S	phenyl	m.p. 151 °C
3	O	cyclohexyl	m.p. 135 °C
4	O	2-Cl-phenyl	m.p. 125 °C
5	O	2,3-diCl-phenyl	m.p. 142 °C
6	O	3,5-diCl-phenyl	m.p. 81 °C
7	O	4-Cl-phenyl	m.p. 180 °C
8	O	2-CF_3-phenyl	m.p. 161 °C
9	O	4-PhO-phenyl	m.p. 162 °C
10	O	2,4-diCl-phenyl	m.p. 90 °C
11	O	3,4-diMeO-phenyl	m.p. 179 °C
12	O	2,6-xylyl	m.p. 175-7 °C
13	O	2,6-diCl-phenyl	m.p. 178 °C
14	O	3-tolyl	m.p. 165-7 °C
15	O	3,4-diCl-phenyl	m.p. 132 °C
16	O	3-CF_3-phenyl	^1H N.M.R δ (ppm) 4.7 (2H, d), 6.7 (1H, s), 7.2 (1H, d), 7.3 (1H, t), 7.5 (1H, d), 7.6 (1H, s), 7.85 (1H, s), 8.1 (1H, s), 8.5 (1H, s).
17	O	3-MeO-phenyl	m.p. 118 °C
18	O	4-CF_3-phenyl	m.p. 167-8 °C
19	O	4-CN-phenyl	m.p. 209-13 °C
20	O	2-MeO-phenyl	m.p. 144-6 °C
21	O	4-MeO-phenyl	m.p. 192 °C
22	O	2,4-diMeO-phenyl	m.p. 172 °C
23	O	3-NO_2-phenyl	m.p. 94 °C
24	O	2-NO_2-phenyl	m.p. 137-9 °C
25	O	4-tolyl	m.p. 201 °C

Cmp	X	A^2	Characterising data
26	O	2-tolyl	m.p. 138 °C
27	O	3-Br-phenyl	m.p. 104 °C
28	O	4-Br-phenyl	m.p. 181-5 °C
29	S	cyclopropyl	m.p. 102 °C
30	S	2-Cl-phenyl	m.p. 126 °C
31	S	4-Cl-phenyl	m.p. 153 °C
32	S	3,5-diCl-phenyl	m.p. 179 °C
33	S	2,4-diCl-phenyl	m.p. 160 °C
34	S	2,3-diCl-phenyl	m.p. 170-2 °C
35	S	2-CF_3-phenyl	m.p. 140-2 °C
36	S	2,6-xylyl	m.p. 170-3 °C
37	S	3,4-diMeO-phenyl	m.p. 172-5 °C
38	S	3-PhO-phenyl	m.p. 152-3 °C
39	S		oil
40	S	3-MeS-phenyl	m.p. 142-3 °C
41	S	3-methylcarbonylphenyl	m.p. 160 °C
42	S	3-Cl-4-tolyl	m.p. 163 °C
43	S	3-($PhSO_2$)-phenyl	m.p. 195-8 °C
44	S	4-But-phenyl	m.p. 108-9 °C
45	S	3-CF_3-phenyl	m.p. 158-60 °C
46	S	4-NMe_2-phenyl	m.p. 177-81 °C
47	S	4-$MeSO_2$-phenyl	m.p. 160-3 °C
48	S	4-MeS-phenyl	m.p. 172-6 °C
49	S	6-NO_2-2-naphthyl	m.p. 194-8 °C
50	S	2-tolyl	m.p. 158-60 °C
51	S	2-Pr^i-phenyl	m.p. 124-7°C
52	S	2,6-diCl-phenyl	m.p. 186-9 °C
53	S	4-Br-phenyl	m.p. 143-5 °C
54	S	2-Cl-4-$MeSO_2$-phenyl	m.p. 176-8 °C
55	S	4-Me-2-NO_2-phenyl	m.p. 136-9 °C
56	S	2-Cl-4-$PrSO_2$-phenyl	m.p. 166-9 °C
57	S	4-(4-Me-	m.p. 185-9 °C

Cmp	X	A^2	Characterising data
		benzylsulfonyl)phenyl	
58	S	4-(4-Cl-phenylthio)phenyl	m.p. 147-50 °C
59	S	cyclohexyl	^{1}H N.M.R δ (ppm) 1.1-2.1 (10H, m), 3.8 (1H, br), 5.0 (2H, br), 6.5 (1H, br), 7.4 (1H, br), 8.0 (1H, s) and 8.7 (1H, s)
60	S	4-PhO-phenyl	m.p. 109-10 C
61	S	2-PhO-phenyl	^{1}H N.M.R δ (ppm) 8.63 (1H, s), 8.1 (2H, d), 7.95 (1H, s), 7.65 (1H, s), 7.65 (1H, d), 7.4-6.9 (8H, m) and 5.1 (2H, d).
62	S	3-Pr^{i}O-phenyl	^{1}H N.M.R δ (ppm) 8.6 (1H, s), 8.18 (1H, s), 8.04 (1H, br), 7.95 (1H, s), 7.35 (1H, t), 6.86 (3H, d), 5.1 (2H, d), 4.58 (1H, m), 1.35 (6H, d)
63	S	3,4-diCl-phenyl	^{1}H N.M.R δ (ppm) 8.6 (1H, s), 8.0 (1H, s), 7.5-7.1 (3H, m), 4.9 (2H, d), 4.7 (2H, d)
64	S	2-MeO-phenyl	^{1}H N.M.R δ (ppm) 8.64 (1H, s), 8.05 (1H, br), 7.9 (1H, s), 7.85 (1H, br), 7.5 (1H, d), 7.25 (1H, dd), 7.0 (2H, dd), 5.1 (2H, d), 3.85 (3H, s)

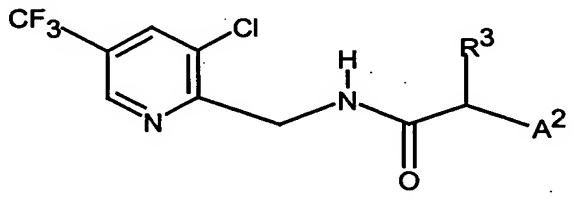
Example 2

N-[(3-Chloro-5-trifluoromethyl-2-pyridyl)methyl]-2-nitrophenylacetamide (Compound 108)

To a stirred suspension of 2-nitrophenylacetic acid (0.36 g) in dry toluene (5 ml) at room temperature was added phosphoryl chloride (0.37 g) and stirring was continued overnight. Meanwhile a solution of the amine was prepared. (3-Chloro-5-trifluoromethyl-2-pyridyl)methylamine hydrochloride (0.49 g) in dry toluene (5 ml) and triethylamine (1.23 g) was stirred at room temperature for 1 hour and then filtered. The solid was washed with dry toluene and the combined filtrates were added dropwise to the above suspension of acid chloride with ice-cooling. After addition, the mixture was stirred at room temperature overnight. Dichloromethane was added and the mixture was washed with water. The

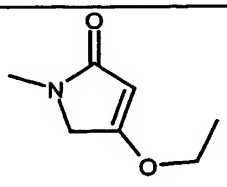
aqueous layer was separated and back-extracted with dichloromethane. The combined organic xtracts were washed with saturated sodium bicarbonate solution, then brine, then dried ($MgSO_4$), and the solvent removed. The resulting residue was purified by silica gel chromatography eluting with ethyl acetate/light petroleum (b.p. 40-60 °C) to give the title product, m.p. 123-4 °C.

The following compounds of formula Ig (see Table B), i.e. compounds of general formula I where A^1 is 3-Cl-5-CF_3-2-pyridyl, R^1 and R^2 are hydrogen and L is -NHC(=O)CH(R^3)-, may be prepared by methods analogous to those of Example 2.



(Ig)

Table B

Cmp	R^3	A^2	m.p. (°C)
101	H	thienyl	oil
102	ethyl	phenyl	oil
103	MeC(=O)O-	phenyl	oil
104	H	2,4-diMeO-phenyl	oil
105	phenyl	phenyl	oil
106	Cl	phenyl	102-3
107	H	2,6-diCl-phenyl	136-9
108	H	2-NO_2-phenyl	123-4
109	H	3-Cl-phenyl	88-9
110	H	2-Cl-6-F-phenyl	133-4
111	Pr^i	1-imidazolyl	120
112	H		134

The ^1H N.M.R. data of those compounds in Table B which were not solid at room temperature are presented below.

Compound 101

^1H N.M.R. ($CDCl_3$) δ(ppm) 3.9 (2H, s), 4.7 (2H, d), 7.0 (2H, d), 7.1 (1H, br.s), 7.3 (2H, m), 7.9 (1H, s) and 8.7 (1H, s)

Compound 102

^1H N.M.R. ($CDCl_3$) δ(ppm) 0.9 (3H, t), 1.9 (1H, m), 2.25 (1H, m), 3.4 (1H, t), 4.7 (2H, qd), 6.9 (1H, bs), 7.2-7.4 (5H, m), 7.9 (1H, s), 8.65 (1H, s).

Compound 103

^1H N.M.R. ($CDCl_3$) δ(ppm) 2.25 (3H, s), 4.75 (2H, d), 6.2 (1H, s), 7.4 (3H, m), 7.5 (2H, m), 7.7 (1H, bs), 8.0 (1H, s), 8.75 (1H, s).

Compound 104

^1H N.M.R. ($CDCl_3$) δ(ppm) 3.65 (2H, s), 3.8 (3H, s), 3.9 (3H, s), 4.7 (2H, d), 6.8-7.0 (3H, m), 7.1 (1H, bs), 7.9 (1H, s), 8.75 (1H, s).

Compound 105

^1H N.M.R. ($CDCl_3$) δ(ppm) 4.8 (2H, d), 5.1 (1H, s), 7.1-7.4 (1H, m), 7.9 (1H, s) and 8.65 (1H, s).

Example 3

Methyl 2-[(2-chlorobenzyl)amino]-3-[3-chloro-5-(trifluoromethyl)-2-pyridyl]propanoate

(Compound 218)

To a mixture of the product from stage h) below in tetrahydrofuran (12 ml) and methanol (4 ml) was added 1M sodium methoxide in methanol (4 drops) and the mixture was heated at 65 °C for 3 days. The mixture was filtered and the solid washed successively with portions (5 ml) of methanol, dichloromethane and methanol. The combined filtrates were evaporated to give the title product, ^1H

N.M.R δ (ppm) 8.63 (1H, s), 7.89 (1H, s), 7.15-7.35 (4H, m), 3.92 (3H, m), 3.74 (3H, s), 3.42 (2H, d).

Preparation of starting materials

a) *N-(tert*-Butoxycarbonyl)glycine cesium salt

To a mixture of *N-(tert*-butoxycarbonyl)glycine (42.0 g) in water (250 ml) was added cesium carbonate (39.1 g). The mixture was stirred at room temperature for 10 minutes. The water was removed by azeotropic distillation with toluene to give the title product.

b) Attachment to Solid Support

Merrifield resin (61.2 g) was swollen in dry dimethylformamide (350 ml). The product from stage a) (75.5. g) was added followed by more dry dimethylformamide (250 ml) and the mixture was stirred at 65 °C overnight. On cooling, the mixture was filtered and the solid washed successively with portions (400 ml) of dimethylformamide, dimethylformamide/water (1:1), water, dichloromethane, methanol, dichloromethane and finally methanol (x2). The solid was dried in a vacuum oven overnight.

c) Treatment with Trifluoroacetic Acid

To a mixture of the product from stage b) (76.2 g) swollen in dry dichloromethane (660 ml) was added trifluoroacetic acid (220 ml) and the mixture was stirred at room temperature for 5.5 hours. The mixture was filtered and the solid was washed successively with portions (400 ml) of dichloromethane (x2), methanol, dichloromethane and methanol (x2). The resin was dried overnight.

d) Treatment with Benzophenone Imine

To a mixture of the product from stage c) (76.6 g) swollen in dry dichloromethane (650 ml) was added benzophenone imine (61 ml) in dichloromethane (100 ml) and the mixture stirred overnight. The mixture was filtered and the solid was successively washed with portions (400 ml) of dichloromethane, 20% aqueous tetrahydrofuran (x2), tetrahydrofuran,

dichloromethane, methanol, dichloromethane and methanol (x2). The solid was dried in a vacuum oven overnight.

e) Electrophilic Substitution of the Imine

To a mixture of the product from stage d) (40.4 g) swollen in *N*-methylpyrrolidinone (250 ml) was added phosphazine base P(1)-*tert*-Bu-tris(tetramethylene) (38 ml). 3-Chloro-2-chloromethyl-5-trifluoromethylpyridine (42.4 g) was then added and the mixture was stirred at room temperature overnight. The mixture was filtered and the solid was washed successively with portions (200 ml) of *N*-methylpyrrolidinone (x2), dichloromethane (x2) methanol, dichloromethane and methanol (x2). The solid was dried in a vacuum oven overnight.

f) Conversion of Imine to Amine Hydrochloride

To a mixture of the product from stage e) (52.1 g) swollen in tetrahydrofuran (750 ml) was added 2M hydrochloric acid (250 ml). The mixture was stirred for 4 hours and then filtered. The solid was washed successively with portions (250 ml) of tetrahydrofuran (x2), dichloromethane (x2), methanol, dichloromethane, methanol and diethyl ether. The solid was dried in a vacuum oven overnight.

g) Conversion to Amine

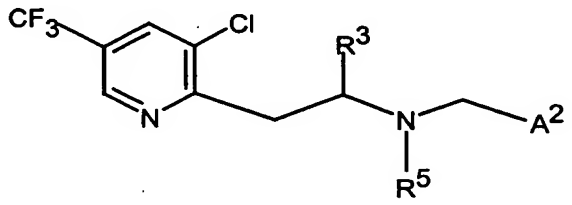
A mixture of the product from stage f) in 10% triethylamine in dichloromethane was stirred at room temperature for 2 hours. The mixture was filtered and the solid was stirred in 5% triethylamine in dichloromethane for 1 hour. The mixture was filtered again, and the solid was stirred in dichloromethane for 1 hour. The mixture was filtered and the solid washed successively with portions of methanol, dichloromethane, methanol and diethyl ether (x2). The solid was dried in a vacuum oven overnight.

h) Conversion of Primary Amin to Secondary Amine

A mixture of the product from stage g) (4.2 mmol) in trimethylorthoformate (90 ml) was treated with 2-chlorobenzaldehyd (42 mmol) and stirred at room temperatur for 6 hours. Sodium

cyanoborohydride (42 mmol) followed by acetic acid (1.3 ml) was then added and the mixture stirred at room temperature for 16 hours. The mixture was filtered and the solid was washed successively with portions of aqueous tetrahydrofuran, tetrahydrofuran, methanol, dichloromethane, methanol, dichloromethane, methanol and diethyl ether (x2). The solid was dried in a vacuum oven overnight.

The following compounds of formula Ih (see Table C), i.e. compounds of general formula I where A^1 is 3-Cl-5-CF_3-2-pyridyl, R^1 and R^2 are hydrogen and L is -$CH(R^3)N(R^5)CH_2$-, may be prepared by methods analogous to those of Example 3.



(Ih)

Table C

Cmp	R^3	R^5	A^2	Characterising data
201	EtNHC(=O)-	H	phenyl	^{1}H N.M.R δ (ppm) 8.61 (1H, s), 7.8 (1H, s), 7.43 (1H, m), 7.1-7.3 (5H, m), 3.1-3.3 (7H, m), 1.16 (3H, t)
202	EtNHC(=O)-	MeC(=O)-	phenyl	^{1}H N.M.R δ (ppm) 8.64 (1H, s), 7.73 (1H, s), 7.27 (3H, m), 7.10 (2H, m), 6.53 (1H, m), 5.82 (1H, t), 4.70 (2H, m), 3.43 (2H, m), 3.20 (2H, m), 2.14 (3H, s) and 1.03 (3H, t).
203	EtNHC(=O)-	H	3-tolyl	^{1}H N.M.R δ (ppm) 8.63 (1H, s), 7.86 (1H, s), 7.54 (1H, m), 7.13 (1H, m), 7.06 (1H, m), 6.98 (2H, m), 3.1-3.8 (7H, m), 2.34 (3H, s), 1.17 (3H, t)
204	MeOC(=O)-	H	3-t lyl	*m/z* (ES) 387 $(M+H)^+$
205	EtOC(=O)-	H	3-tolyl	^{1}H N.M.R δ (ppm) 8.67 (1H, s), 7.88 (1H, s), 7.18 (1H, m), 7.02 (2H, m),

Cmp	R^3	R^5	A^2	Characterising data
				4.10 (2H, q), 3.78 (3H, m), 3.37 (2H, m), 2.32 (3H, s), 1.24 (3H, t)
206	EtNHC(=O)-	H	4-MeO-phenyl	*m/z* (ES) 416 $(M+H)^+$
207	EtNHC(=O)-	H	2-Cl-phenyl	*m/z* (ES) 420 $(M+H)^+$
208	EtNHC(=O)-	H	2,6-diF-phenyl	*m/z* (ES) 422 $(M+H)^+$
209	EtNHC(=O)-	H	2-NO_2-phenyl	*m/z* (ES) 431 $(M+H)^+$
210	EtNHC(=O)-	H	2-naphthyl	*m/z* (ES) 436 $(M+H)^+$
211	EtNHC(=O)-	H	3,4-diMeO-phenyl	*m/z* (ES) 446 $(M+H)^+$
212	EtNHC(=O)-	H	2-CF_3-phenyl	*m/z* (ES) 454 $(M+H)^+$
213	EtNHC(=O)-	H	2,4-diCl-phenyl	*m/z* (ES) 454 $(M+H)^+$
214	EtNHC(=O)-	H	3-PhO-phenyl	*m/z* (ES) 478 $(M+H)^+$
215	MeNHC(=O)-	H	2-Cl-phenyl	*m/z* (ES) 406 $(M+H)^+$
216	MeNHC(=O)-	H	3-NO_2-phenyl	*m/z* (ES) 417 $(M+H)^+$
217	MeOC(=O)-	H	4-MeO-phenyl	*m/z* (ES) 403 $(M+H)^+$
218	MeOC(=O)-	H	2-Cl-phenyl	^1H N.M.R δ (ppm) 8.63 (1H, s), 7.89 (1H, s), 7.15-7.35 (4H, m), 3.92 (3H, m), 3.74 (3H, s), 3.42 (2H, d)
219	MeOC(=O)-	H	2,6-diF-phenyl	^1H N.M.R δ (ppm) 8.62 (1H, s), 7.83 (1H, s), 7.20 (1H, m), 6.34 (2H, m), 3.73 (3H, m), 3.68 (3H, s), 3.28 (2H, d)
220	MeOC(=O)-	H	2-NO_2-phenyl	*m/z* (ES) 418 $(M+H)^+$
221	MeOC(=O)-	H	2-naphthyl	*m/z* (ES) 423 $(M+H)^+$
222	MeOC(=O)-	H	3,4-diMeO-phenyl	*m/z* (ES) 433 $(M+H)^+$
223	MeOC(=O)-	H	2-CF_3-phenyl	*m/z* (ES) 441 $(M+H)^+$
224	MeOC(=O)-	H	2,6-diCl-phenyl	^1H N.M.R δ (ppm) 8.62 (1H, s), 7.89 (1H, s), 7.1-7.35 (3H, m), 3.83 (3H, m), 3.72 (3H, s), 3.39 (2H, m)
225	MeOC(=O)-	H	3-PhO-phenyl	^1H N.M.R δ (ppm) 8.62 (1H, s), 7.83 (1H, s), 6.3-7.2 (9H, m), 3.79 (3H, m), 3.71 (3H, s), 3.38 (2H, m)
226	EtOC(=O)-	H	phenyl	^1H N.M.R δ (ppm) 8.62 (1H, s), 7.88 (1H, s), 7.1-7.3 (5H, m), 4.18 (2H, q), 3.79 (3H, m), 3.38 (2H, m), 1.21 (3H, t)

Cmp	R^3	R^5	A^2	Characterising data
227	EtOC(=O)-	H	4-MeO-phenyl	^{1}H N.M.R δ (ppm) 8.63 (1H, s), 7.88 (1H, s), 7.12 (2H, d), 6.79 (2H, d), 4.10 (2H, q), 3.81 (3H, s), 3.73 (3H, m), 3.38 (2H, m), 1.23 (3H, t)
228	EtOC(=O)-	H	2-Cl-phenyl	^{1}H N.M.R δ (ppm) 8.62 (1H, s), 7.86 (1H, s), 7.1-7.4 (4H, m), 4.19 (2H, q), 3.89 (3H, m), 3.40 (2H, m), 1.23 (3H, t)
229	EtOC(=O)-	H	2,6-diF-phenyl	^{1}H N.M.R δ (ppm) 8.61 (1H, s), 7.82 (1H, s), 7.21 (1H, m), 6.82 (2H, t), 4.16 (2H, q), 3.91 (3H, m), 3.38 (2H, d), 1.22 (3H, t)
230	EtOC(=O)-	H	2-NO_2-phenyl	^{1}H N.M.R δ (ppm) 8.62 (1H, s), 7.87 (2H, m), 7.35-7.55 (3H, m) 4.20 (2H, m), 4.08 (2H, m), 3.36 (m), 3.37 (2H, m), 1.14 (3H, t)
231	EtOC(=O)-	H	2-naphthyl	^{1}H N.M.R δ (ppm) 8.61 (1H, s), 7.25-7.9 (8H, m), 3.8-4.3 (5H, m), 3.41 (2H, m), 1.24 (3H, t)
232	EtOC(=O)-	H	3,4-diMeO-phenyl	^{1}H N.M.R δ (ppm) 8.64 (1H, s), 7.89 (1H, s), 6.78 (3H, m), 4.19 (2H, q), 3.86 (3H, s), 3.81 (3H, s), 3.75 (2H, m), 3.39 (2H, m), 1.24 (3H, t)
233	EtOC(=O)-	H	2-CF_3-phenyl	^{1}H N.M.R δ (ppm) 8.66 (1H, s), 7.91 (1H, s), 7.3-7.65 (4H, m), 4.21 (2H, m), 3.98 (3H, m), 3.41 (3H, m), 1.26 (3H, t)
234	EtOC(=O)-	H	2,4-diCl-phenyl	^{1}H N.M.R δ (ppm) 8.64 (1H, s), 7.89 (1H, s), 7.1-7.35 (3H, m), 4.20 (2H, m), 3.86 (3H, m), 3.40 (2H, m), 1.24 (3H, t)
235	EtOC(=O)-	H	3-PhO-phenyl	^{1}H N.M.R δ (ppm) 8.62 (1H, s), 7.83 (1H, s), 6.8-7.4 (9H, m), 4.18 (2H, q), 3.77 (3H, m), 3.38 (2H, m), 1.22 (3H, t)

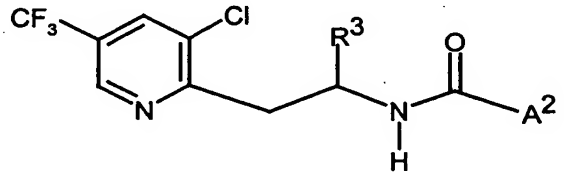
Cmp	R^3	R^5	A^2	Characterising data
236	MeNHC(=O)-	H	2-naphthyl	*m/z* (ES) 422 $(M+H)^+$
237	MeNHC(=O)-	H	2,4-diCl-phenyl	*m/z* (ES) 440 $(M+H)^+$
238	MeNHC(=O)-	H	3-PhO-phenyl	*m/z* (ES) 464 $(M+H)^+$
239	MeOC(=O)-	H	phenyl	*m/z* (ES) 373 $(M+H)^+$

Example 4

Methyl 2-bromobenzoylamino-3-(3-chloro-5-trifluoromethyl-2-pyridyl)proprionate (Compound 321)

To a mixture of the product from Example 3 stage g) in dry dichloromethane was added triethylamine and the solution was stirred for 15 minutes. 2-Bromobenzoyl chloride in dry dichloromethane was added, and the mixture was stirred at room temperature overnight. The mixture was filtered and the solid was washed successively with portions (125 ml) of dichloromethane (x2), methanol, dichloromethane, methanol, dichloromethane (x2), methanol and diethyl ether (x2). The solid was dried in a vacuum oven overnight. To this solid in tetrahydrofuran (12 ml) and methanol (4 ml) was added 1M sodium methoxide in methanol (4 drops) and the mixture was heated at 65 °C for 3 days. The mixture was filtered and the solid washed successively with portions (5 ml) of methanol, dichloromethane and methanol. The combined filtrates were evaporated to give the title product, ^{1}H N.M.R δ (ppm) 8.62 (s), 7.31 (s), 7.56 (2H, m), 7.37 (m), 7.29 (m), 5.40 (m), 3.76 (3H, s) and 3.71 (2H, m).

The following compounds of formula Ij (see Table D); i.e. compounds of general formula I where A^1 is 3-Cl-5-CF_3-2-pyridyl, R^1 and R^2 are hydrogen and L is -CH(R^3)NHC(=O)-, may be prepared by methods analogous to those of Example 4.



(Ij)

Table D

Cmp	R^3	A^2	Characterising data
301	EtNHC(=O)-	4-MeO-phenyl	^{1}H N.M.R δ (ppm) 8.66 (1H, s), 7.91 (1H, s), 7.89 (1H, d), 7.77 (2H, d), 6.94 (2H, d), 6.32 (1H, d), 6.32 (1H, d), 5.21 (1H, m), 3.97 (3H, s), 3.55 (2H, m), 3.25 (2H, m), 1.08 (3H, t)
302	EtNHC(=O)-	2,6-diCl-phenyl	^{1}H N.M.R δ (ppm) 8.60 (1H, s), 7.91 (1H, s), 7.2-7.4 (3H, m), 6.74 (1H, m), 5.33 (1H, m), 3.62 (2H, m), 3.29 (2H, m), 1.12 (3H, t)
303	EtNHC(=O)-	cyclopropyl	*m/z* (ES) 364 $(M+H)^+$
304	EtNHC(=O)-	phenyl	*m/z* (ES) 400 $(M+H)^+$
305	EtNHC(=O)-	cyclohexyl	*m/z* (ES) 406 $(M+H)^+$
306	EtNHC(=O)-	4-Cl-phenyl	*m/z* (ES) 435 $(M+H)^+$
307	EtNHC(=O)-	3-NO_2-phenyl	*m/z* (ES) 445 $(M+H)^+$
308	EtNHC(=O)-	3-CF_3-phenyl	*m/z* (ES) 468 $(M+H)^+$
309	EtNHC(=O)-	4-PhO-phenyl	*m/z* (ES) 476 $(M+H)^+$
310	EtNHC(=O)-	2-Br-phenyl	*m/z* (ES) 478 $(M+H)^+$
311	MeNHC(=O)-	cyclopropyl	^{1}H N.M.R δ (ppm) 8.67 (1H, s), 7.92 (1H, s), 6.70 (1H, br), 5.09 (1H, m), 3.46 (2H, m), 2.80 (3H, m), 1.42 (1H, m), 0.97 (2H, m), 0.81 (2H, m)
312	MeNHC(=O)-	cyclohexyl	^{1}H N.M.R δ (ppm) 8.64 (1H, s), 7.91 (1H, s), 7.08 (1H, d), 6.68 (1H, m), 5.04 (1H, q), 3.43 (2H, m), 2.73 (3H, m), 1.2-2.3 (11H, m)
313	MeNHC(=O)-	2,6-diCl-phenyl	^{1}H N.M.R δ (ppm) 8.62 (1H, s), 7.85 (1H, s), 7.46 (1H, d), 7.34 (3H, m), 4.82 (1H, m), 5.36 (1H, m), 3.62 (2H, m), 2.84 (3H, d)
314	MeNHC(=O)-	phenyl	*m/z* (ES) 386 $(M+H)^+$
315	MeNHC(=O)-	4-MeO-phenyl	*m/z* (ES) 416 $(M+H)^+$
316	MeNHC(=O)-	4-biphenylyl	*m/z* (ES) 462 $(M+H)^+$
317	MeOC(=O)-	phenyl	^{1}H N.M.R δ (ppm) 8.95 (1H, s), 7.93 (2H, m), 7.26 (3H, m), 5.38 (1H, m), 3.76 (3H, s), 3.70 (2H, m)
318	MeOC(=O)-	cyclohexyl	^{1}H N.M.R δ (ppm) 8.66 (1H, s), 7.91 (1H, s), 6.63 (1H, d), 5.18 (1H, m), 3.71 (3H, s), 3.57 (2H, m), 1.2-2.15 (11H, m)

Cmp	R^3	A^2	Characterising data
319	MeOC(=O)-	2,6-diCl-phenyl	^{1}H N.M.R δ (ppm) 8.60 (1H, s), 7.95 (1H, s), 7.28 (3H, m), 1.03 (1H, d), 5.42 (2H, m), 3.74 (5H, m)
320	MeOC(=O)-	4-biphenylyl	^{1}H N.M.R δ (ppm) 8.72 (1H, s), 7.92 (1H, s), 7.35-7.9 (9H, m), 5.39 (1H, m), 3.78 (3H, s), 3.70 (2H, m)
321	MeOC(=O)-	2-Br-phenyl	^{1}H N.M.R δ (ppm) 8.62 (1H, s), 7.31 (1H, s), 7.56 (2H, m), 7.37 (1H, m), 7.29 (1H, m), 5.40 (1H, m), 3.76 (3H, s), 3.71 (2H, m)
322	EtOC(=O)-	cyclohexyl	^{1}H N.M.R δ (ppm) 8.64 (1H, s), 7.92 (1H, s), 6.64 (1H, d), 5.16 (1H, m), 4.18 (2H, m), 3.59 (2H, m), 0.3-2.2 (11H, m), 1.22 (3H, t)
323	EtOC(=O)-	4-MeO-phenyl	^{1}H N.M.R δ (ppm) 8.69 (1H, s), 7.91 (1H, s), 7.77 (2H, d), 7.38 (1H, d), 8.92 (2H, d), 5.32 (1H, m), 4.20 (2H, m), 3.34 (3H, t), 3.67 (2H, m)
324	EtOC(=O)-	3-CF_3-phenyl	^{1}H N.M.R δ (ppm) 8.68 (1H, s), 8.06 (1H, s), 7.96 (2H, m), 7.30 (2H, m), 7.60 (2H, m), 5.36 (1H, m), 4.21 (2H, m) 3.71 (2H, m), 1.23 (3H, t),
325	EtOC(=O)-	2,6-diCl-phenyl	^{1}H N.M.R δ (ppm) 8.62 (1H, s), 7.94 (1H, s), 7.26 (3H, m), 7.04 (1H, d), 5.41 (1H, m), 4.21 (2H, m), 3.73 (2H, m), 1.22 (3H, t)
326	EtOC(=O)-	2-Br-phenyl	^{1}H N.M.R δ (ppm) 8.64 (1H, s), 7.93 (1H, s), 7.57 (1H, m), 7.33 (1H, m), 7.26 (1H, m), 5.39 (1H, m), 4.22 (2H, m), 3.75 (2H, m), 1.23 (3H, t)
327	MeOC(=O)-	cyclopropyl	*m/z* (ES) 351 $(M+H)^+$
328	MeOC(=O)-	4-MeO-phenyl	*m/z* (ES) 417 $(M+H)^+$
329	MeOC(=O)-	4-Cl-phenyl	*m/z* (ES) 421 $(M+H)^+$
330	MeOC(=O)-	3-NO_2-phenyl	*m/z* (ES) 432 $(M+H)^+$
331	MeOC(=O)-	3-CF_3-phenyl	*m/z* (ES) 455 $(M+H)^+$
332	EtOC(=O)-	cyclopropyl	*m/z* (ES) 365 $(M+H)^+$
333	EtOC(=O)-	phenyl	*m/z* (ES) 401 $(M+H)^+$
334	EtOC(=O)-	4-Cl-phenyl	*m/z* (ES) 435 $(M+H)^+$
335	EtOC(=O)-	3-NO_2-phenyl	*m/z* (ES) 446 $(M+H)^+$
336	EtOC(=O)-	4-biphenylyl	*m/z* (ES) 477 $(M+H)^+$

Cmp	R^3	A^2	Characterising data
337	MeNHC(=O)-	4-Cl-phenyl	*m/z* (ES) 420 $(M+H)^+$
338	MeNHC(=O)-	3-NO_2-phenyl	*m/z* (ES) 431 $(M+H)^+$
339	MeNHC(=O)-	3-CF_3-phenyl	*m/z* (ES) 454 $(M+H)^+$
340	MeNHC(=O)-	2-Br-phenyl	*m/z* (ES) 464 $(M+H)^+$

Example 5

N-[2-(3-Chloro-5-trifluoromethyl-2-pyridyl)ethyl]-2,6-dichlorobenzamide (Compound 401)

To a suspension of 2-(3-chloro-5-trifluoromethyl-2-pyridyl)ethylammonium chloride (0.2 g) in dry dichloromethane at 10 °C was added 2,6-dichlorobenzoyl chloride (0.13 ml) followed by dropwise addition of dry triethylamine (0.3 ml). The mixture was warmed with stirring to 22 °C over 18 hours. The mixture was evaporated on to flash silica. Chromatography over silica eluting with 20-50% diethyl ether in light petroleum (b.p. 40-60 °C) gave the title product, m.p. 103-5 °C.

Preparation of Starting Material

2-(3-Chloro-5-trifluoromethyl-2-pyridyl)ethylammonium chloride

To a solution of the product from Example 6 (1.0 g) in ethanol (10 ml) was added hydrazine hydrate (0.15 ml) and the mixture was heated under reflux for 3 hours. Concentrated hydrochloric acid (1 ml) was added and the mixture was heated at 80 °C for 1 hour to give a filterable precipitate. The mixture was cooled to 10 °C, filtered and then evaporated to dryness *in vacuo*. The residue was dissolved in water (10 ml) and then basified to greater than pH 10 using 2M aqueous sodium hydroxide solution. The aqueous solution was ether extracted (3x15 ml) and the combined extracts were brine washed (2x10 ml). The organic extract was dried ($MgSO_4$), the filtrate acidified with 6M hydrogen chloride in diethyl ether (5 ml) and evaporated to dryness. The solid residue was triturated with ethyl ether, filtered and dried *in vacuo* to give the title compound, m.p. 188-92 °C.

Example 6

2-{2-[3-Chloro-5-(trifluoromethyl)-2-pyridyl]ethyl}-1,3-isoindolinedione

(Compound 402)

To a solution of the product from Example 7 (5.63 g) in glacial acetic acid (50 ml) was added 48% hydrogen bromide solution (10 ml) and the mixture was heated at 120 °C for 2 hours. The cold mixture was evaporated *in vacuo* and partitioned between water (100 ml) and dichloromethane (100 ml). The aqueous layer was separated and extracted with dichloromethane (2x10 ml). The combined extracts were water washed (2x20 ml), dried ($MgSO_4$), and evaporated onto flash silica. Chromatography over silica eluting with 3-30% diethyl ether in light petroleum (b.p 40-60 °C) gave the title compound, m.p. 147-8 °C.

Example 7

Diethyl 2-[3-chloro-5-(trifluoromethyl)-2-pyridyl]-2-[(1,3-dioxo-2,3-dyhydro-1*H*-2-isoindolyl)methyl]malonate

(Compound 403)

To a suspension of 60% sodium hydride (0.65 g) in dry dimethylformamide (20 ml) at 0 °C was added a solution of diethyl 2-(3-chloro-5-trifluoromethyl-2-pyridyl)malonate (5 g) in dry dimethylformamide (10 ml) and the mixture was stirred for 15 minutes. A solution of *N*-bromomethylphthalimide (3.55 g) in dry dimethylformamide (10 ml) was added dropwise and the mixture was warmed with stirring to 22 °C over 18 hours. Glacial acetic acid (1 ml) was added and the mixture was poured into cold water (500 ml). The aqueous solution was extracted with diethyl ether (3x150 ml) and the combined extract was water washed (3x100 ml). The organic extract was dried ($MgSO_4$) and evaporated to give a crude product. Trituration with diethyl ether/light petroleum (b.p. 40-60 °C) (1:1) gave the title compound, m.p. 159-61 °C.

Preparation of Starting Materials

Diethyl 2-(3-chloro-5-trifluorom thyl-2-pyridyl)malonate

To a suspension of 60% sodium hydrid in mineral oil (5.28 g) in dry dimethylformamide (50 ml) at 0 °C was added a solution of diethyl malonate (10 ml) in dry dimethylformamide (25 ml) and the mixture was

stirred for 30 minutes. A solution of 2,3-dichloro-5-(trifluoromethyl)pyridine (9.8 ml) in dry dimethylformamide (10 ml) was added dropwise and the mixture warmed with stirring to 22 °C over 18 hours. Acetic acid (7.5 ml) in diethyl ether (20 ml) was added dropwise and the mixture was stirred until hydrogen evolution had ceased. The mixture was diluted with diethyl ether (600 ml) and then water washed (3x200 ml). The organic extract was dried ($MgSO_4$) and evaporated onto flash silica. Chromatography over silica eluting with 0-20% diethyl ether in light petroleum (b.p. 40-60 °C) gave the title compound, ^1H N.M.R. ($CDCl_3$) δ(ppm) 1.28 (6H, t, 2x CH_3CH_2), 4.30 (4H, q, 2xCH_2CH_3), 5.24 (1H, s, $CH(CO_2Et)_2$), 7.96 (1H, s, py-H), 8.74 (1H, s, py-H).

Example 8

(Compound 501)

To a solution of *O*-{[3-chloro-5-(trifluoromethyl)-2-pyridyl]methyl} hydroxylamine (0.4 g) and triethylamine (0.18 g) in tetrahydrofuran (20 ml) was added 2,6-dichlorobenzoyl chloride (0.37 g). The reaction mixture was stirred for 20 hours at room temperature before filtering the solution and evaporation of the filtrate. The resulting residue was redissolved in ethyl acetate and washed successively with dilute hydrochloric acid, saturated sodium bicarbonate solution and water. The organic phase was dried, filtered and evaporated to yield the crude product which was further purified by silica gel column chromatography to give the title compound.

Preparation of Starting Material

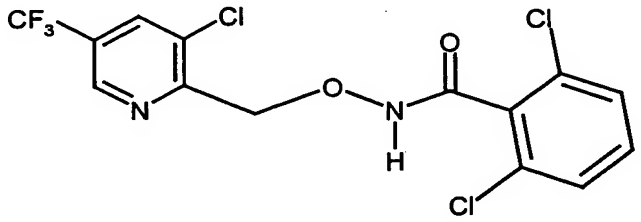
O-{[3-Chloro-5-(trifluoromethyl)-2-pyridyl]methyl} hydroxylamine

To a solution of *N*-hydroxyphthalimide (3.55 g) in dimethylformamide (50 ml) was added potassium carbonate (3.0 g) to give a thick yellow suspension which was stirred for 1 hour. 3-Chloro-2-chloromethyl-5-trifluoromethylpyridine (5.0 g) was added and the reaction stirred at room temperature for 20 hours. The mixtur was filtered and the filtrate poured into water. The resulting white solid was isolated by filtration, washed with water, redissolved in ethyl acetate and the organic solution dried and evaporated to yield the intermediate phthalimide as a white solid. The

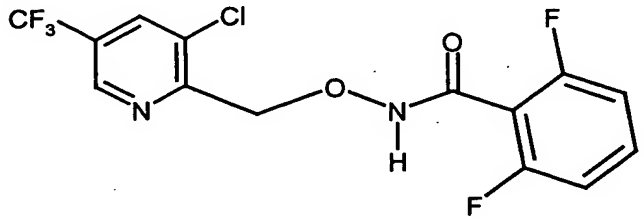
phthalimide (2.0 g) was dissolved in methanol (20 ml) and the resulting solution treated with hydrazine hydrate (0.42 g). The reaction was left to stand for 19 hours before heating at reflux for 3 hours to yield a white precipitate. The reaction mixture was filtered and the methanol filtrate evaporated. The residue was treated with diethyl ether and refiltered. Evaporation of the filtrate yielded the title compound as a green yellow oil.

The following compounds of general formula I where A^1 is 3-Cl-5-CF_3-2-pyridyl, R^1 and R^2 are hydrogen and L is -O-NHC(=O)-, may be prepared by methods analogous to those of Example 8.

Compound 501 m.p. 127-9 °C



Compound 502 m.p. 108-10 °C



Test Example

Compounds were ass ssed for activity against one or more of the following:

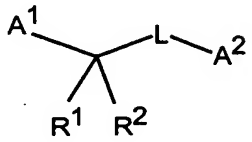
Phytophthora infestans: late tomato blight
Plasmopara viticola: vine downy mildew
Erysiphe graminis f. sp. tritici: wheat powdery mildew
Pyricularia oryzae: rice blast
Leptosphaeria nodorum: glume blotch

Aqueous solutions or dispersions of the compounds at the desired concentration, including a wetting agent, were applied by spray or by drenching the stem base of the test plants, as appropriate. After a given time, plants or plant parts were inoculated with appropriate test pathogens before or after application of the compounds as appropriate, and kept under controlled environmental conditions suitable for maintaining plant growth and development of the disease. After an appropriate time, the degree of infection of the affected part of the plant was visually estimated. Compounds are assessed on a score of 1 to 3 where 1 is little or no control, 2 is moderate control and 3 is good to total control. At a concentration of 500 ppm (w/v) or less, the following compounds scored 2 or more against the fungi specified.

Phytophthora infestans:	31 and 105-7.
Plasmopara viticola:	50, 55, 104, 105, 201, 215, 221, 222, 224, 225, 227, 230, 232, 233, 234, 235 and 328.
Erysiphe graminis f. sp. tritici:	4, 25, 26, 39, 40, 44, 101, 201, 214, 304, 305, 306, 308, 310, 312 and 313.
Pyricularia oryzae:	111, 112, 306 and 312.
Leptosphaeria nodorum:	13, 105, 107, 108, 201, 229, 232, 238, 317 and 336.

Claims

1 The use of a compound of general formula I and salts thereof as phytopathogenic fungicides



(I)

where

A^1 is 2-pyridyl or its *N*-oxide, each of which may be substituted by up to four groups at least one of which is haloalkyl;

A^2 is heterocyclyl or carbocyclyl, each of which may be substituted;

L is a 3-atom linker, selected from the list: $-N(R^5)C(=X)N(R^6)-$, $-N(R^5)C(=X)CH(R^3)-$, $-CH(R^3)N(R^5)CH(R^4)-$, $-CH(R^3)N(R^5)C(=X)-$, $-N(R^3)CH(R^4)C(=X)-$ or $-O-N(R^5)C(=X)-$; wherein A^1 is attached to the left hand side of linker L;

where R^1, R^2, R^3 and R^4, which may be the same or different, are R^b, cyano, nitro, halogen, $-OR^b$, $-SR^b$ or optionally substituted amino;

R^5 and R^6 which may be the same or different, are R^b, cyano or nitro; or any R^1, R^3 or R^5 group, together with the interconnecting atoms, can form a 3-, 4- 5- or 6-membered ring with any R^2, R^4 or R^6 or any R^1, R^2, R^3, R^4, R^5 or R^6 group, together with the interconnecting atoms can form a 5- or 6-membered ring with A^2;

X is oxygen or sulfur;

wherein R^b is alkyl, alkenyl, alkynyl, carbocyclyl or heterocyclyl, each of which may be substituted, or hydrogen or acyl.

2 A pesticidal composition comprising at least one compound as claimed in claim 1 in admixture with an agriculturally acceptable diluent or carrier.

3 A method of combating pests at a locus infested or liable to be infested therewith, which comprises applying to the locus a compound as claimed in claim 1.